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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/018,677	05/15/2002	Nicole Suci-Foca	58332-A-PCT-US/JPW/FHB	2458

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EXAMINER

BELYAVSKYI, MICHAEL A

ART UNIT

PAPER NUMBER

1644

DATE MAILED: 04/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

10/018,677

Applicant(s)

SUCIU-FOCA ET AL.

Examiner

Michail A. Belyavskyi

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 26 January 2005.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-57 is/are pending in the application.
- 4a) Of the above claim(s) 1-33, 37 and 39- 57 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 34, 36 and 38 is/are rejected.
- 7) ☒ Claim(s) 35 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☒ Other: See Continuation Sheet.

Continuation of Attachment(s) 6). Other: Notice to comply with sequence requirements.

DETAILED ACTION

1. Claims 1-57 are pending.

2. Applicant's election with traverse of Group XVI, claims 34-36 and 38 in the reply filed on 01/26/2005 is acknowledged. Applicant traverse the Restriction Requirement on the grounds that the search of Groups I-XXV together would not constitute a serious search burden on the examiner and that search of the claims of Group XVI would provide useful information for the claims of Groups I- XV and XVII-XXV.

This is not found persuasive because the MPEP 803 (August 2001) states that "For purposes of the initial requirement, a serious burden on the examiner may be prima facie shown if the examiner shows by appropriate explanation either separate classification, separate status in the art, or a different field of search". The Restriction Requirement enunciated in the previous Office Action meets this criteria and therefore establishes that serious burden is placed on the examiner by the examination of more than one Group. The Inventions are distinct for reasons elaborated in paragraphs 3-5 of the previous Office Action and above

The requirement is still deemed proper and is therefore made FINAL.

3. Claims 1-33, 37 and 39- 57 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 34-36 and 38 read on a method of inducing anergic T helper cells comprising a step of incubating APC with allospecific T suppressor cells are under consideration in the instant application.

4. The specification on page 1, should be amended to reflect the status of the parent 09/333,809 application.

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5. This application contains sequences disclosures on page 88, line 9 and in Figures 27A – 27H that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures.

Applicant is reminded of the sequence rules which require a submission for all sequences of 10 or more nucleotides or 4 or more amino acids (see 37 CFR 1.821-1.825) and is also requested to carefully review the submitted specification for any and all sequences which require compliance with the rules.

Applicant is reminded to amend the specification and the claims accordingly.

6. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention *to which the claims are directed*.

7. Applicant asserts that an IDS was submitted with the prior application 09/333,809. However, these citations have been crossed out as said references cited in said parent application cannot be found. Applicant is invited to resubmit such references to complete the instant file. The examiner apologizes for any inconvenience to applicant for having to resubmit such documents.

8. The lengthy specification has not been checked to the extent necessary to determine the presence of all possible minor errors. For example on page 4, line 34 and on page 104, line 34 the word “T_h” is misspelled and on page 118, line 24, the word “tyrosine” is misspelled. Applicant's cooperation is requested in correcting any errors of which Applicant may become aware in the specification.

9. Claim 34 is objected to because of the following informalities: The word “tyrosine” is misspelled. Appropriate correction is required.

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10. Claim 35 is objected to because of the following informalities: an extra comma is present following the word "(MIR7)".

Appropriate correction is required.

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 34, 36 and 38 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inducing anergic T helper cells which comprises overexpressing in the APC mRNA which encodes at least one monocytes inhibitory receptor (MIR) wherein said MIR is selected from the group consisting of ILT4 (MIR-10), ILT2 (MIR7) and ILT3 does not reasonably provide enablement for a method of inducing anergic T helper cells which comprises overexpressing in the APC mRNA which encodes at least *any* one of monocytes inhibitory receptor (MIR), as recited in claim 34. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The specification does not enable one of skill in the art to practice the invention as claimed without undue experimentation.

The claims as written encompass the genus of monocytes inhibitory receptor (MIR) wherein overexpression of said MIR in APC can be used in the method of inducing anergic T helper cells.

Factors to be considered in determining whether undue experimentation is required to practice the claimed invention are summarized *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)). The factors most relevant to this rejection are the scope of the claim, the amount of direction or guidance provided, the limited working examples, the unpredictability in the art and the amount of experimentation required to enable one of skill in the art to practice the claimed invention.

Applicant discloses that the invention is based on the results of micro-arrays assay that identify the specific genes which are differentially expressed in APC that have been exposed to allospecific Ts. Applicant disclosed that very specific MIR genes i.e. ILT4, ILT2 and ILT3 were among the only 10-15 genes that have been up-regulated (see page 118, lines 5-30 in particular). Applicant further disclosed that these molecules interact with MHC-class I molecules via Ig-like domains and regulate negatively the activation of APC, through recruiting an inhibitory signaling molecule, tyrosine phosphatase SHP-1 (see page 118, lines 25-30 in

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particular). Upregulation of the expression of said molecules is the essential mechanism in a method of inducing anergic T helper cells (see overlapping pages 118 and 119 in particular).

Applicant has not taught how overexpression of any MIR in APCs, other than the specific one as recited in claim 35, can be used in the method of inducing anergic T helper. Applicant has not provided sufficient biochemical information (e.g. structural characteristics, amino acid composition, physicochemical properties, etc) that distinctly identifies any MIR overexpression of which in APCs transmits negative inhibitory signals and can be used in the method of inducing anergic T helper cells, other than specific MIR encompassed by claim 35. Moreover, Papanikolaou et al., (Human Immunology, 2004, v.65, pages 700-705) teach that there are differences in binding affinity among MIR to their receptors and these differences would result in variation in the strength of tolerizing signals that are generated by said MIRs in APCs (see entire document, overlapping pages 704-705 in particular). Similarly, Chang et al., (Immunol. Nature, 2002, v.3 pages 237-243) teach that only upregulation of specific MIR, i.e. IL3 and IL4 have an immunoregulatory effect upon APCs

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed method of inducing anergic T helper cells which comprises overexpressing in the APC mRNA which encodes at least *any* one of monocytes inhibitory receptor (MIR), in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18 (CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

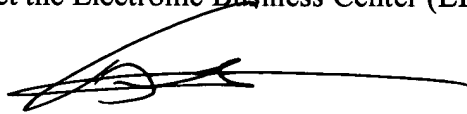
13. Claim 35 is objected to as being dependent upon a rejected base claim 34, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

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14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskiy whose telephone number is 571/272-0840. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/272-0841.

The fax number for the organization where this application or proceeding is assigned is 571/273-8300

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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March 24, 2005.